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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,586	10/27/2003	Ekambar R. Kandimalla	HYB-005US5	3762

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EXAMINER
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HORNING, MICHELLE S

ART UNIT	PAPER NUMBER
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1648

MAIL DATE	DELIVERY MODE
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10/02/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/694,586	<b>Applicant(s)</b> KANDIMALLA ET AL.	
	<b>Examiner</b> Michelle Horning	<b>Art Unit</b> 1648	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 July 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 20, 21, 39 and 40 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 20-21 AND 39-40 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

This office action is responsive to communication filed 7/11/2007. The status of the claims is as follows: claims 20-21 and 39-40 are under current examination.

#### *Withdrawn Rejection*

The following rejection has been withdrawn due to amendments of the claims:

1. 35 USC 103 (Chaix et al and Lin).

#### ***Claim Rejections - 35 USC § 112-MAINTAINED***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claims 20-21 and 39-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.** The claims read upon an immunostimulatory oligonucleotide comprising (in part) a 3'-3' linker and one or two accessible 5' ends, provided that the oligonucleotide is not complementary to the gag or tat gene of HIV-1. As noted in the previous office action, it is not clear how such an oligonucleotide can be complementary to an HIV-1 gene given the claimed oligonucleotide includes a 3'-3' linker.

Applicants' response was considered but not found persuasive. While it may be clear to one of ordinary skill in the art that this would be interpreted as "neither

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sequence on the left nor right side of the 3'-3' linker would be complementary to the gag or tat gene of HIV-1" (see Remarks, page 4) following the thought of the oligonucleotide's multiple directionalities, the claim does not state that and is open to other interpretations. Instead, the claim states the following: "provided that the oligonucleotide is not complementary to the gag or tat gene of HIV-1". This suggests the oligonucleotide as a whole, which would then include the 3'-3' linker. Thus, this rejection is maintained.

***Claim Rejections - 35 USC § 103-NECESSITATED BY AMENDMENTS***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chaix et al (1996) and US Patent # 6562798 (Schwartz).** The limitations of the rejected claims above are as follows:

20. An immunostimulatory oligonucleotide compound, comprising: an immunostimulatory dinucleotide of formula CpG, wherein C is non-natural pyrimidine nucleoside and G is a natural or non-natural purine nucleoside, and wherein p is an internucleotide linkage selected from the group consisting of phosphodiester, phosphorothioate and phosphorodithioate; a 3'-3' linkage; and one or two accessible 5' ends; provided that the oligonucleotide is not complementary to the gag or tat gene of HIV-1.

21. The immunostimulatory oligonucleotide compound of claim 20, which oligonucleotide comprises two accessible 5' ends.

Chaix et al discloses oligonucleotide sequences that include a 3' -3' linker and two accessible 5' ends (see sequences 2 and 4 in Table 1). Chaix et al discloses a marked increase in the stability of these sequences in contrast to the 5'-3' sequences (see Conclusion and Figure 1). Chaix et al teaches using sequences that are complementary to either the gag or tat gene of HIV-I. While Chaix et al teach an increase in sequence stability, this reference does not disclose immunostimulatory sequences comprising CpG wherein the C is a non-natural pyrimidine.

Swartz teaches compositions comprising immunostimulatory oligonucleotide sequences in which at least one base has been substituted with a base modified by the

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addition to C-5 and/or C-6 on cytosine with an electron-withdrawing moiety (see abstract). More specifically, Swartz describes an immunostimulatory oligonucleotide comprises having the CpG dinucleotide where the C is modified. Figures 1-4 illustrate the structure of the 5-cytosine substituted CpG dinucleotide and their immunostimulatory effects. It would have been obvious to one of ordinary skill in the art to combine the teachings of Chaix et al and Swartz in order to modify the CpG containing immunostimulatory sequences as taught by Chaix et al and use 3' -3' linkers in immunostimulatory sequences disclosed by Swartz. One would have been motivated to do so, as taught by Chaix et al (see last paragraph), in order to increase the oligonucleotides' stability against nuclease-mediated degradation in contrast to 5' -3' oligonucleotides. Of note, this paper teaches that there is a marked increase in the structural integrity of an oligonucleotide by inserting a 3'-3' linker and this insertion would have been obvious for any oligonucleotide of *any function*. There would have been a reasonable expectation of success given that the success is well described in the prior art by both Chaix et al and Swartz, and the underlying techniques are widely used. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

### ***Double Patenting-MAINTAINED***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

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from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

**Claims 20-21 and 39-40 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/174448.** Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an oligonucleotide comprising a linker and two accessible 5' ends.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Claims 20-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/234074.** Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an oligonucleotide comprising a linker and two accessible 5' ends.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Claims 20-21 and 39-40 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/234075.** Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an oligonucleotide comprising a linker and two accessible 5' ends.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.



**Claims 20-22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/174002.** Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an oligonucleotide comprising a linker, a non-natural pyrimidine and two accessible 5' ends.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Claims 20-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/173983.** Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an oligonucleotide comprising a linker and two accessible 5' ends.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Claims 20-21 and 39-40 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/173794.** Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an oligonucleotide comprising a linker and two accessible 5' ends.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Claims 20-21 and 39-40 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/174282.** Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an oligonucleotide comprising a linker and two accessible 5' ends.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Claims 20-21 and 39-40 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/173938.** Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an oligonucleotide comprising a linker and two accessible 5' ends.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Claims 20-21 and 39-40 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/174450.** Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an oligonucleotide comprising a linker and two accessible 5' ends.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Claims 20-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 39-40 of copending Application No. 11/270805.** Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an oligonucleotide comprising a linker and two accessible 5' ends.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Claims 20-21 and 39-40 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 7 of copending Application No. 10/757345.** Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an oligonucleotide comprising a linker and two accessible 5' ends.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Claims 20-22 and 39-40 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 6, 7, 10 and 24 of copending Application No. 10/279684.** Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an oligonucleotide comprising a linker and two accessible 5' ends.

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants have indicated that they will consider filing a Terminal Disclaimer or other necessary action at a later time. This is not a proper response and thus, these rejections are maintained.

### ***Conclusions***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

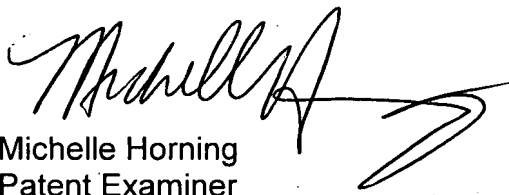
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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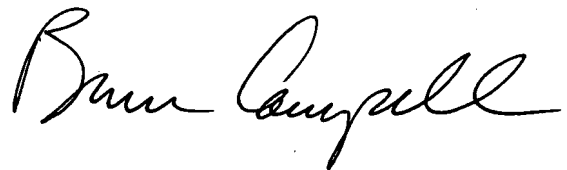
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michelle Horning whose telephone number is 571-272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Michelle Horning  
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